UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/660,131	09/11/2003	David H. Munn	M0351-287806	6907

7590 12/11/2007

Cynthia B. Rothschild
Kilpatrick Stockton LLP
1001 West Fourth Street
Winston-Salem, NC 27101-2400

EXAMINER	
DEBERRY, REGINA M	

ART UNIT	PAPER NUMBER
1647	

MAIL DATE	DELIVERY MODE
12/11/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/660,131	MUNN ET AL.	
	Examiner	Art Unit	
	Regina M. DeBerry	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE *3* MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 August 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 3-6* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 3-6* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *10/07*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Status of Application, Amendments and/or Claims

The amendment filed 28 August 2007 has been entered in full. Claims 2, 7-48 are canceled. Claims 1, 3-6 are under examination.

In view of the papers filed 28 August 2007, the inventorship in this nonprovisional application has been changed by the deletion of Stephen C. Peiper. The application will be forwarded to the Office of Initial Patent Examination (OIPE) for issuance of a corrected filing receipt, and correction of Office records to reflect the inventorship as corrected.

Information Disclosure Statement

The information disclosure statement(s)(IDS) filed 24 October 2007 was received and complies with the provisions of 37 CFR §§1.97 and 1.98. It has been placed in the application file and the information referred to therein has been considered as to the merits.

Withdrawn Objections And/Or Rejections

The rejection to claims 1, 3-8, 13, 14, 16-20, 47, 48 under 35 U.S.C. first paragraph, scope of enablement, as set forth at pages 3-6 of the previous Office Action (08 May 2007), is *withdrawn* in view of the amendment (28 August 2007).

The rejection to claims 1, 3-8, 10, 13, 14, 16-20, 47, 48 under 35 U.S.C. 112, second paragraph, as set forth at pages 6-7 of the previous Office Action (08 May 2007), is *withdrawn* in view of the amendment (28 August 2007).

Claim Rejections - 35 USC § 103(a)

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1, 3-6 are rejected under 35 U.S.C. 103(a) as being unpatentable over Brennan et al. (US Patent Application Publication US 2003/0140361 A1) in view of Yang et al. (reference submitted by Applicant; Science Vol. 286, October 15, 1999), Bell et al. (J. Exp Med., Volume 190, Number 10, pages 1417-1425, Nov. 1999), Kleeff et al. (Int. J. Cell, Volume 81, pages 650-657, 1999) and Friberg et al. (reference submitted by Applicant; Int. J. Cancer, 101, pages 151-155, July 26, 2002).

Brennan et al. teach methods and agents that modulate receptor CCR6. **Brennan et al. teach the *in vivo* use of CCR6 antibodies for the inhibition of abnormal CCR6 gene activity (para 0033 and 0147).** Brennan et al. do not teach dentritic cells (DC), which express elevated levels of indoleamine 2,3-dioxygenase

(IDO) or administering antibodies to CCR6 *in vivo* to reduce the recruitment of IDO+ DCs to a tumor or a tumor-draining lymph node.

Yang et al. (reference submitted by Applicant; Science Vol. 286, October 15, 1999) teach beta-defensins as antimicrobial peptides, which are chemotactic for immature dendritic cells. Yang et al. teach that beta-defensins are selectively chemotactic for cells stably transfected to express human CCR6. **Yang et al. teach that beta-defensin induced chemotaxis was inhibited by antibodies to CCR6** (page 527, 1st-2nd and Figure 3).

Bell et al. (J. Exp Med., Volume 190, Number 10, pages 1417-1425, Nov. 1999). teach that upon tissue damage, dentritic cells (DCs) capture Ag and subsequently migrate to the lymphoid organs, where they select rare Ag-specific T cells, thereby initiating immune responses. During migration and within the secondary lymphoid organs, DCs undergo maturation from Ag-capturing cells to antigen presenting cells (APCs). Bell et al. teach that tumor immunity can be viewed as a three-step process that includes presentation of tumor-associated Ags, selection and activation of tumor associated Ags specific T cells and homing of the antigen associated Ags T cells to the tumor site and elimination of tumor cells. **Bell et al. teach that tumors may escape immune surveillance due to alteration at each of these steps (page 1417).** Bell et al. teach that immature DC infiltration is associated with a high expression of macrophage inflammatory protein (MIP-3) alpha by tumor cells and that recent studies demonstrated the expression of CCR6 on immature DCs. Bell et al. teach that the accumulation of immature DCs within the tumor bed may be dependent on the

expression of MIP-3 alpha by tumor cells (page 1423). Bell et al. teach that immature DC in the tumor environment appeared much higher than in the normal breast epithelium, suggesting increased homing and infiltration. Bell et al. teach that this may be best explained by the high levels of intra-tumoral MIP-3 alpha, a chemokine that was recently shown to specifically attract immature DC and is now found to be expressed within the tumor epithelium (abstract, page 1424, 1st paragraph). **Thus, Bell et al. teach that immature DCs infiltration is associated with a high expression of MIP-3 alpha by tumor cells, that immature DCs express CCR6 and that the accumulation of immature DCs within the tumor bed may be dependent of the expression of MIP-3 alpha by tumor cells.**

Kleeff et al. (Int. J. Cancer, Volume 81, 650-657, 1999) teach that MIP-3 alpha is a chemotactic cytokine, which signals through the receptor CCR6. **Kleeff et al. teach the overexpression of MIP-3 alpha in pancreatic tumors and in several other cancer cell lines. Kleeff et al. teach that pancreatic cancer cells as well as cancer cells within the tumor mass express the CCR6 receptor** (abstract and page 655, 3rd paragraph).

Friberg et al. (reference submitted by Applicant, Int. J. Cancer, 101, pages 151-155, July 26, 2002) teach that the enzyme IDO can be immunosuppressive. **Friberg et al. teach that indoleamine 2,3-dioxygenase (IDO) contributes to tumor cell evasion of T cell mediated rejection. Friberg et al. teach that various tumor cell types are known to express IDO.** Friberg et al. teach IDO may be an immunosuppressive protein produced by mononuclear cells that invade tumors and

tumor draining lymph nodes. Friberg et al. teach that their studies provide evidence for a novel mechanism whereby tumors evade rejection by the immune system, and suggest the possibility that inhibiting IDO may be developed as an anti-cancer immunotherapeutic strategy (abstract; page 151 and page 155).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to modify the method of administering CCR6 antibodies *in vivo* for the inhibition of abnormal CCR6 gene activity, as taught by Brennan et al., by formulating it as a method to reduce the recruitment of IDO+ DCs to a tumor or tumor draining lymph node with a reasonable expectation of success. The motivation and expected success is provided by Yang, Bell, Kleeff, and Friberg. Yang et al. teach that beta-defensin induced chemotaxis is inhibited by antibodies to CCR6. Bell et al. teach that immature DCs express CCR6 and that immature DC infiltration is associated with high expression of MIP-3 alpha by tumor cells. Kleeff et al. teach the overexpression of MIP-3 alpha in pancreatic tumors and that pancreatic cancer cells as well as cancer cells within the tumor mass express the CCR6 receptor. Friberg et al. teach that IDO contributes to tumor cell evasion of T cell mediated rejection and that various tumor cell types are known to express IDO.

One skilled in the art would be motivated to administer CCR6 antibodies to block the MIP-3 alpha signal by tumor cells to prevent chemotaxis/accumulation of IDO+ DCs expressing CCR6 to a tumor or a tumor draining lymph node expressing MIP-3 alpha.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to REGINA M. DEBERRY whose telephone number is (571)272-0882. The examiner can normally be reached on 9:00 a.m.-6:30 p.m.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Manjunath N. Rao can be reached on (571) 272-0939. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Marianne P. Allen/
Primary Examiner, Art Unit 1647

RMD
12/5/07